REMARKS

Status of the Claims

Claims 1, 14-17, 19, 21-23, 38 and 54-77 are in the application.

Claims 1, 14-17, 19, 21-23, 54-63, 65-74, 76 and 77 were rejected.

Claims 38, 64 and 75 have been withdrawn from consideration.

By way of this amendment, claim 77 has been amended and claims 21-23, 54, 61-63, 65, 72-74 and 76 have been canceled.

Upon entry of this amendment, claims 1, 14-17, 19, 38, 55-60, 64, 66-71, 75 and 77 will be pending.

Summary of the Amendment

Claim 77 has been amended to delete repetitive phrases arising from an obvious typographical error.

Claims 21-23, 54, 61-63, 65, 72-74 and 76 have been canceled without prejudice.

No new matter has been added.

Request for Withdrawal of Finality of the Rejections

Applicants respectfully request that the finality of the rejection be reconsidered and withdrawn. The new rejection under 35 U.S.C. 103(a) is asserted to be necessitated by Applicants' amendment. The new rejection is directed to claim 1 and to new claim 77.

Claim 1 was previously amended to recite specific types of immunomodulating proteins.

New claim 77 recites the elected species and was added following the election of species requirement made after the filing of Applicants' amendment and reply to the previous Official Action on the merits.

The rejection as applied to claim 1 could have been applied to claim 1 prior to the amendment. The amendment did not necessitate the new grounds for rejection. The rejected

subject matter was included in claim 1 prior to the amendment and the rejection as currently applied could have been made earlier. Applicants respectfully request that the finality of the rejection be reconsidered and withdrawn.

Election/Restriction

Claims 38, 64 and 75 have been withdrawn from consideration as being directed to non-elected subject matter. Applicants respectfully request that upon finding generic claims from which claims 38, 64 and 75 to be allowable, claims 38, 64 and 75 will be rejoined, examined and allowed.

Claim Rejections under 35 USC § 112, second paragraph

Claims 66 and 77 stand rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Claim 66, which is dependent on claim 1, is asserted to indefinite because it is asserted that recitation of the phrase "the non-IgE protein" is unclear whether such reference is directed to the "the non-IgE protein" referred to on lines 3-4 of claim 1 or the "the non-IgE protein" referred to on lines 6-7 of claim 1. Applicants respectfully urge that claim 66 is clear and definite and one skiled in the art would readily recognize what subject matter is being claimed.

The limitation of non-IgE protein in claim 66 applies to the non-IgE protein in claim 1. While claim 1 itself includes two alternative limitations, i.e. a non-IgE protein from the same species as the IgE signal peptide or a non-IgE protein that is one of several expressly recited immunomodulatory proteins, the additional limitation in claim 66 is clear in indicating that the non-IgE protein that is from the same species as the IgE signal peptide is an immunomodulatory protein or the non-IgE protein is one of several expressly recited immunomodulatory proteins without limitation to whether or not it is from the same species. Claim 66 is clear and definite.

Claim 77 has been rejected as being indefinite due to the inclusion of certain repetitive language. The objected to language was included due to an obvious typographical error and has been deleted by the amendment. As amended, claim 77 is clear and definite.

Applicants respectfully request that the rejection Applicants respectfully request that the rejection of claims 66 and 77 under 35 U.S.C. §112, second paragraph, be withdrawn.

Claim Rejection Under 35 U.S.C. § 112, first paragraph

Claims 21-23, 54, 61-63, 65, 72-74, and 76 stand rejected under 35 U.S.C. §112, first paragraph, for allegedly failing the enablement requirement. Applicants respectfully disagree. However, to advance prosecution of the other pending claims, Applicants have canceled claims 21-23, 54, 61-63, 65, 72-74, and 76 without prejudice. The rejection of claims 21-23, 54, 61-63, 65, 72-74, and 76 under 35 U.S.C. §112, first paragraph, is moot.

Claim Rejections under 35 USC § 102

Weiner

Claims 1, 14-17, 19, 21-23, 54-63, 65-74 and 76 stand rejected under 35 U.S.C. 102(a) and 102(e) as allegedly being anticipated by Weiner, *et. al.*, US 2002/0123099 A1 (hereinafter "Weiner"). Applicants traverse the rejection and respectfully request that the rejection be withdrawn.

Claims 21-23, 54, 61-63, 65, 72-74, and 76 have been canceled without prejudice and the rejection is moot.

With respect to the rejection of claims 1, 14-17, 19, 55-60 and 66-71, Applicants respectfully point out that Weiner does not anticipate the claims.

As noted in the Official Action, claim 1 refers to "a nucleic acid sequence" which is either

> a nucleic acid sequence that encodes
> a fusion protein that consists of a
> non-IgE protein sequences linked to

> an IgE signal peptide that is from the same species as the non-IgE protein

or

> a nucleic acid sequence that encodes a fusion protein that consists of a non-IgE protein sequences linked to an IgE signal peptide, wherein the non-IgE protein is an immunomodulating protein selected from the group consisting of cytokines, chemokines, cellular death receptors, cellular adhesion molecules, cellular growth factors, cellular growth factor receptors, protein kinases and enzymes or functional fragment thereof.

Applicants respectfully urge that Weiner discloses neither. Weiner discloses constructs having coding sequences for a fusion protein comprising a human Ig signal peptide linked to a West Nile virus capsid protein. Such a fusion protein comprising a human Ig signal peptide linked to a West Nile virus capsid protein is not

> a fusion protein that consists of a non-IgE protein sequences linked to an IgE signal peptide that is from the same species as the non-IgE protein

as set forth in claim 1. The Ig signal disclosed in Weiner is a human Ig signal and the non-IgE protein disclosed in Weiner is a viral protein. The non-IgE protein disclosed in Weiner is not from the same species as the non-IgE signal peptide as required by the first of the two alternatives in claim 1.

Likewise, a fusion protein comprising a human Ig signal peptide linked to a West Nile virus capsid protein is not

> a fusion protein that consists of a non-IgE protein sequences linked to an IgE signal peptide, wherein the non-IgE protein is an

> immunomodulating protein selected from the group consisting of cytokines, chemokines, cellular death receptors, cellular adhesion molecules, cellular growth factors, cellular growth factor receptors, protein kinases and enzymes or functional fragment thereof.

as set forth in claim 1. The non-IgE protein disclosed in Weiner is a viral capsid protein. The non-IgE protein disclosed in Weiner is not a cytokine, chemokine, cellular death receptor, cellular adhesion molecule, cellular growth factor, cellular growth factor receptor, protein kinase, enzyme or functional fragment thereof as required by the second of the two alternatives in claim 1.

Claims 1, 14-17, 19, 55-60 and 66-71 are not anticipated be Weiner. Applicants respectfully request that the rejection of claims 1, 14-17, 19, 21-23, 54-63, 65-74 and 76 under 35 U.S.C. 102(a) and 102(e) as allegedly being anticipated by Weiner, as applied to claims 1, 14-17, 19, 55-60 and 66-71, be withdrawn.

Yang 1

Claims 1, 14, 16, 17, 19, 21, 22, 38, 54-56, 58-62, 64-67, 69-74, and 76 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Yang, *et. al.*, *Journal of Infectious Disease*; 184(7): 809-16, 2001 (hereinafter "Yang 1").

Claims 21, 22, 54, 61, 62, 65, 72-74, and 76 have been canceled without prejudice and the rejection is moot.

With respect to the rejection of claims 1, 14, 16, 17, 19, 38, 55, 56, 58-60, 64, 66, 67 and 69-71, Applicants respectfully point out that Yang 1 does not anticipate the claims.

As noted in the Official Action, claim 1 refers to "a nucleic acid sequence" which is either

> a nucleic acid sequence that encodes a fusion protein that consists of a non-IgE protein sequences linked to

> an IgE signal peptide that is from the same species as the non-IgE protein

or

> a nucleic acid sequence that encodes a fusion protein that consists of a non-IgE protein sequences linked to an IgE signal peptide, wherein the non-IgE protein is an immunomodulating protein selected from the group consisting of cytokines, chemokines, cellular death receptors, cellular adhesion molecules, cellular growth factors, cellular growth factor receptors, protein kinases and enzymes or functional fragment thereof.

Applicants respectfully urge that Yang 1 discloses neither. Yang 1 discloses constructs having coding sequences for a fusion protein comprising a human Ig signal peptide linked to a West Nile virus capsid protein. Such a fusion protein comprising a human Ig signal peptide linked to a West Nile virus capsid protein is not

> a fusion protein that consists of a non-IgE protein sequences linked to an IgE signal peptide that is from the same species as the non-IgE protein

as set forth in claim 1. The Ig signal disclosed in Yang 1 is a human Ig signal and the non-IgE protein disclosed in Yang 1 is a viral protein. The non-IgE protein disclosed in Yang 1 is not from the same species as the non-IgE signal peptide as required by the first of the two alternatives in claim 1.

Likewise, a fusion protein comprising a human Ig signal peptide linked to a West Nile virus capsid protein is not

> a fusion protein that consists of a non-IgE protein sequences linked to an IgE signal peptide, wherein the non-IgE protein is an

> immunomodulating protein selected from the group consisting of cytokines, chemokines, cellular death receptors, cellular adhesion molecules, cellular growth factors, cellular growth factor receptors, protein kinases and enzymes or functional fragment thereof.

as set forth in claim 1. The non-IgE protein disclosed in Yang 1 is a viral capsid protein. The non-IgE protein disclosed in Yang 1 is not a cytokine, chemokine, cellular death receptor, cellular adhesion molecule, cellular growth factor, cellular growth factor receptor, protein kinase, enzyme or functional fragment thereof as required by the second of the two alternatives in claim 1.

Claims 1, 14, 16, 17, 19, 55, 56, 58-60, 66, 67 and 69-71 are not anticipated by Yang 1. Applicants respectfully request that the rejection of claims 1, 14, 16, 17, 19, 21, 22, 38, 54-56, 58-62, 64-67, 69-74, and 76 under 35 U.S.C. 102(b) as allegedly being anticipated by Yang 1, as applied to claims 1, 14, 16, 17, 19, 55, 56, 58-60, 66, 67 and 69-71, be withdrawn.

Yang 2

Claims 1, 14, 16, 17, 19, 21, 22, 54-56, 58-62, 65-67, 69-74 and 76 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Yang, *et. al.*, *Emerg Infect Dis*; 8(12):1379-84, 2002 (hereinafter "Yang 2").

Claims 21, 22, 54, 61, 62, 65, 72-74, and 76 have been canceled without prejudice and the rejection is moot.

With respect to the rejection of claims 1, 14, 16, 17, 19, 55, 56, 58-60, 66, 67 and 69-71, Applicants respectfully point out that Yang 1 does not anticipate the claims.

As noted in the Official Action, claim 1 refers to "a nucleic acid sequence" which is either

> a nucleic acid sequence that encodes a fusion protein that consists of a non-IgE protein sequences linked to

> an IgE signal peptide that is from the same species as the non-IgE protein

or

> a nucleic acid sequence that encodes a fusion protein that consists of a non-IgE protein sequences linked to an IgE signal peptide, wherein the non-IgE protein is an immunomodulating protein selected from the group consisting of cytokines, chemokines, cellular death receptors, cellular adhesion molecules, cellular growth factors, cellular growth factor receptors, protein kinases and enzymes or functional fragment thereof.

Applicants respectfully urge that Yang 2 discloses neither. Yang 2 discloses constructs having coding sequences for a fusion protein comprising a human Ig signal peptide linked to a West Nile virus capsid protein. Such a fusion protein comprising a human Ig signal peptide linked to a West Nile virus capsid protein is not

> a fusion protein that consists of a non-IgE protein sequences linked to an IgE signal peptide that is from the same species as the non-IgE protein

as set forth in claim 1. The Ig signal disclosed in Yang 2 is a human Ig signal and the non-IgE protein disclosed in Yang 2 is a viral protein. The non-IgE protein disclosed in Yang 2 is not from the same species as the non-IgE signal peptide as required by the first of the two alternatives in claim 1.

Likewise, a fusion protein comprising a human Ig signal peptide linked to a West Nile virus capsid protein is not

> a fusion protein that consists of a non-IgE protein sequences linked to an IgE signal peptide, wherein the non-IgE protein is an

> immunomodulating protein selected from the group consisting of cytokines, chemokines, cellular death receptors, cellular adhesion molecules, cellular growth factors, cellular growth factor receptors, protein kinases and enzymes or functional fragment thereof.

as set forth in claim 1. The non-IgE protein disclosed in Yang 2 is a viral capsid protein. The non-IgE protein disclosed in Yang 2 is not a cytokine, chemokine, cellular death receptor, cellular adhesion molecule, cellular growth factor, cellular growth factor receptor, protein kinase, enzyme or functional fragment thereof as required by the second of the two alternatives in claim 1.

Claims 1, 14, 16, 17, 19, 38, 55, 56, 58-60, 66, 67 and 69-71 are not anticipated by Yang 1. Applicants respectfully request that the rejection of claims 1, 14, 16, 17, 19, 21, 22, 38, 54-56, 58-62, 64-67, 69-74, and 76 under 35 U.S.C. 102(b) as allegedly being anticipated by Yang 1, as applied to claims 1, 14, 16, 17, 19, 38, 55, 56, 58-60, 66, 67 and 69-71, be withdrawn.

Claim Rejections under 35 USC § 103

Claims 1 and 77 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Yang, *et. al.*, *Journal of Infectious Disease*; 184(7): 809-16, 2001 (hereinafter "Yang 1") in view of Letvin *et al.*, WO 99/16466 (hereinafter "Letvin").

Yang 1 discloses a genetic construct having a coding sequence encoding a human Ig leader sequence linked to a West Nile virus capsid protein.

Letvin disclosed the use of plasmids that encode expressible IL-15 to enhance immune responses.

It is asserted that it would be *prima facie* obvious to one skilled in the art to substitute the West Nile virus capsid protein coding sequence taught in Yang 1 with a coding sequence for IL-15 taught in Letvin. Applicants respectfully disagree.

IL-15 comprises its own signal peptide. Nothing in Yang 1 or Letvin would suggest linking IL-15 to a non-IL-15 signal peptide in view of the existence of its own IL-15 signal peptide. Yang 1 provides a human signal peptide to the viral protein West Nile virus capsid protein in order to provide it with a signal peptide to enhance its expression. IL-15 already includes a signal peptide and one skilled in the art would not see any benefit to add a second signal peptide or use an IgE signal peptide in its place.

One skilled in the art viewing the prior art would not consider the claimed invention obvious. The elected species of the claims invention provides coding sequences for a fusion protein that comprises an IgE signal peptide linked to IL-15 coding sequences.

To combine Yang 1 and Letvin to produce the claimed invention as suggested in the Office Action, one skilled in the art would insert the IL-15 coding sequences in place of the West Nile Virus capsid protein sequence. The resulting construct however would comprise an IgE signal peptide linked to an IL-15 protein that contains its own signal peptide. One skilled in the art would not produce such a construct because one skilled in the art would not include two signal peptides in view of the combined teachings. Such a construct is not obvious.

Similarly, one skilled in the art would not remove the IL-15 signal peptide coding sequences from the coding sequences that encode the mature IL-15 and substitute the IL-15 signal peptide with the West Nile Virus capsid protein sequence. It would not be obvious to one skilled in the art to remove and replace IL-15's own signal peptide with a different signal peptide. The combination of references does not make obvious to one skilled in the art a construct in which the IL-15 signal peptide is excluded and the IgE signal peptide is used in its place. As the data in Examples 3 and 4 of the application detail, the substitution of the IgE signal in place of the IL-15 signal results in constructs with better results compared to the use of Il-15 linked to its own IL-15 signal peptide. The substitution of the IL-15's own signal peptide with one from another protein is itself not obvious. The unexpected improvement observed with Il-15 signal peptide is removed and IgE signal is provided in its place is surprising and unexpected. Accordingly such a construct is not obvious.

In view of the forgoing, the elected subject matter is not obvious in view of the combination of Yang 1 and Letkin. It would not be obvious to one skilled in the art to include coding sequence for an IgE signal peptide in a construct encoding IL-15 that includes an IL-15 signal peptide. It would also not be obvious to one skilled in the art to substitute the coding sequence for an IgE signal peptide in place of the IL-15 signal peptide coding sequences of an IL-15 coding sequence. The resulting construct provides unexpected results, further demonstrating its non-obviousness.

Conclusion

Claims 1, 14-17, 19, 38, 55-60, 64, 66-71, 75 and 77 are in condition for allowance. A notice of allowance is earnestly solicited. Applicants invite the Examiner to contact the undersigned at 610.640.7852 to clarify any unresolved issues raised by this response.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

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